SARS-CoV-2 Impairs Vision

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Abstract
Objectives: affection of the central nervous system and the eyes are increasingly recognised as manifestations of a SARS-CoV-2 infection (COVID-19). This review aims at summarising and discussing recent advances concerning causes and locations of impaired vision due to an infection with SARS-CoV-2.
Methods: Upon a literature search via PubMed and ScholarOne all available publications about COVID-19 patients with impaired vision were retrieved.
Results: Visual impairment in SARS-CoV-2 infected patients may be due to infection of lacrimal glands (dacryoadenitis), conjunctivitis, due to tonic pupils, vitritis, central retinal artery/venous occlusion, retinitis, retinal bleeding, pan-uveitis, anterior ischemic optic neuropathy, optic nerve stroke, optic neuritis, optic peri-neuritis, or occipital ischemic stroke. Visual impairment may be the initial manifestation of SARS-CoV-2.
Conclusions: this mini review shows that impaired vision may be the initial manifestation of COVID-19, that all sections of the visual tract may be affected and causative for visual impairment in COVID-19 patients, and that SARS-CoV-2 manifests along the visual tract with ischemia, focal infection, and immunological reactions.

Key words: visual impairment, optic nerve, retina, occipital lobe, SARS-CoV-2, COVID-19,
Introduction
With ongoing duration of the SARS-CoV-2 pandemic increasing evidence accumulated that infected patients not only manifest in the lungs but also in other organs, either already as onset manifestation [Finsterer, submitted] or later during the disease course [1]. Extra-pulmonary manifestations in the central nervous system (CNS) or the eyes (including the extra-ocular muscles) may lead to transient or permanent impaired vision in one or both eyes [2]. This review aims at summarising and discussing recent advances in the clinical presentation, pathophysiology, diagnosis, treatment, and outcome of SARS-CoV-2 associated impaired vision.

Methods
A literature review in the databases PubMed and Google Scholar using the search terms “optic nerve”, “optic tract”, “chiasm”, “visual radiation”, “visual cortex”, “visual field”, “double vision”, and “occipital lobe”, together with “SARS-CoV-2”, “COVID-19”, and “coronavirus” was conducted. Additionally, reference lists were checked for further articles meeting the search criteria. Excluded were articles in languages other than English, French, Spanish, Italian, or German.

Results
Current data provide evidence that vision in SARS-CoV-2 infected patient can be impaired at several levels (table 1) [3-23]. Ocular causes of impaired vision were more frequent than CNS causes (table 1). However, if the retina and the optic nerve were regarded as part of the CNS, CNS abnormalities were more frequently responsible for impaired vision in COVID-19 patients. Neuro-ophthalmologic causes of visual impairment detected included dacryoadenitis, conjunctivitis, a tonic pupil, myasthenia, vitritis, central retinal artery/venous occlusion (CRAO/CRVO), retinitis, retinal ganglion cell (RGC) dysfunction, retinal bleeding, panuveitis, anterior, ischemic optic neuropathy (AION), optic nerve stroke, optic neuritis, optic perineuritis, ischemic stroke, sinus venous thrombosis, and posterior reversible encephalopathy syndrome (PRES) [3-23]. Thus, impaired vision due to SARS-CoV-2 is multi-causal and multi-locular. Dacryoadenitis has been only reported in a single patient [3]. Conjunctivitis on the contrary, has been much more frequently reported as a complication of COVID-19, and is probably the most frequent ophthalmologic complication of COVID-19 [4]. Since myasthenia exacerbates in about half of the patients with a SARS-CoV-2 infection, it is comprehensible that double vision or
blurred vision may evolve [6]. Vitritis as a complication of COVID-19 has been reported in only two patients so far [7,23].

Retinal abnormalities such as retinitis, CRAO/CRVO, or retinal bleeding are also rare complications of COVID-19 (table 1) [8,12]. CRAO/CRVO are attributed to hypercoagulability frequently complicating COVID-19. Retinal bleeding may be due to hypertension, over-anticoagulation, or hypocoagulability [11].

Affection of the optic nerve is increasingly recognised as a complication of COVID-19. Most prevalent among the optic nerve affections is optic neuritis. Optic neuritis may occur unilaterally [13] or bilaterally [16]. The optic nerve may be the only cranial nerve affected [16] or it may be damaged together with other cranial nerves [24]. Though single or multiple cranial nerve involvement is frequent in Guillain Barre syndrome (GBS) [Finsterer, submitted] affection of the optic nerve has not been reported in patients with SARS-CoV-2 associated GBS [Finsterer, submitted]. Rarely, AION or ischemic stroke of the optic nerve have been reported as complications of COVID-19 (table 1).

Cerebral disease is increasingly recognised as a complication of COVID-19 and may occasionally impair vision in the form of double vision, hemianopia, or visual loos. Cyr et al. described a 61yo SARS-CoV-2 infected male with diabetes, who presented with bilateral visual loss seven days after onset of the viral infection [20]. Since ophthalmologic investigations did not explain visual dysfunction, cerebral computed tomography was carried out revealing bilateral occipital ischemic stroke [20]. A 34yo SARS-CoV-2 infected female with lupus erythematosus, hypertension, and renal insufficiency requiring hemodialysis experienced, sudden painless bilateral visual loss 10 days after admission [20]. Cerebral MRI revealed acute ischemic stroke in the right middle and left posterior cerebral artery territories and chronic stroke in the right posterior cerebral artery territory [20]. Visual impairment in sinus venous thrombosis (SVT) is due to papilledema secondary to raised intracranial pressure (ICP), due to direct ischemic injury of intracranial visual pathways, or direct injury to cranial nerves responsible for ocular motility and pupillary function [21]. Papilledema is found in 28%, visual loss in 13%, and diplopia in 13% of the patients with SARS-CoV-2 associated SVT [21].

Though conceivable, a recent study failed to demonstrate impaired perfusion of the radial peri-papillary capillary plexus [25]. In a case series of four HIV-positive patients who got superinfected with SARS-CoV-2 one experienced retinal detachment one month after discharge from hospital [26]. Since a causal relation between COVID-19 and the retinal detachment could not
unequivocally documented, this patient was not included in the current evaluation [26].

Visual impairment may not only develop after onset of pulmonary or extra-pulmonary COVID-19 but may be the initial manifestation of the infection. Visual impairment as the initial manifestation of the infection has been reported in patients with conjunctivitis [27], panuveitis [13], and optic neuritis [13]. Whether anti-COVID drugs applied to handle the infection may impair vision is so far unknown.

Discussion

This review shows that visual impairment in SARS-CoV-2 infected patients is multi-causal and multi-locular. Visual impairment may be due to infection of lacrimal glands (dacryoadenitis) [3], due to tonic pupils [5], vitritis [7], central retinal artery occlusion [8], retinitis [9], retinal capillary ischemia [10], retinal bleeding [11], panuveitis [13], anterior ischemic optic neuropathy [14], optic nerve stroke [15], optic neuritis [16], optic perineuritis [17], or occipital ischemic stroke [20]. Thus, visual impairment may originate from all possible locations of the optic tract but particularly from affection of the retina and the optic nerve. Pathophysiologically, visual impairment may be due to infection, ischemia, or due to the immunological response. Visual impairment may occur even in the absence of classical pulmonary manifestations of a SARS-CoV-2 infection [13,27]. Thus, patients complaining about impaired vision should be taken serious and investigated also for SAR-CoV-2.

The pathophysiology of optic nerve involvement remains elusive but it can be speculated that it results from intracellular uptake of the virus into neurons at a distal location with consecutive retrograde transport of the virus particles to the brain. An argument for this hypothesis is that in an autopsy study of 43 patients deceased from COVID-19 SARS-CoV-2 viral proteins were detected in cranial nerves originating from the lower brainstem and in isolated cells of the brainstem [28]. Furthermore, virus particles have been repeatedly found in neurons but also axons of cranial nerves in other autopsy studies [29]. Experimental studies indicate that SARS-CoV-2 indeed migrates retrogradually within axons of cranial nerves to the CNS [30].

In conclusion, this review shows that impaired vision may be the initial manifestation of COVID-19, that all sections of the visual tract may be affected, and that SARS-CoV-2 manifests along the visual tract with ischemia, infection, and immunological reactions.
References


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